10 ☒ Please immediately start national examination procedures (35 USC 371(f))

11. ☒ Attached: International Preliminary Examination Report

12. ☐ Preliminary Amendment:

13. ☒ Basic U.S. National fee per Rule 492(a)(1)-(4) was previously timely filed.:

14. **Calculation of remaining fees due (if any):** based on amended claim(s) per above item

☐ 12 (above) or item(s) in PAT-112 (filed previously) ☐ 12 ☐ 14 ☐ 17 ☐ 25

15. **CLAIMS FEES** ☐ previously paid ☒ paid herewith as follows:

				Large/Small Entity		Fee Code
16. Total Effective Claims	17	minus 20 =	0	x $22/$11	+0	966/967
17. Independent Claims	1	minus 3 =	0	x $82/$41	+0	964/965
18. If any proper multiple dependent claim (ignore improper) is present,				$270/$135	+270	968/969
19. Filing Declaration late, fee paid ☐ previously ☒ now				$130/$65	+130	154/254
20.				**SUBTOTAL**	**$400**	
21. **Original due date:** January 2, 1998						
22. **Petition is hereby made** to extend the original due date to cover the date this response is filed for which the requisite fee is attached			(1 mo) (2mos) (3mos) (4mos)	$110/$55 = $400/$200 = $950/$475 = $1510/$755 =	+	115/215 116/216 117/217 118/218
23. If "non-English" box 3 is X'd, add Rule 17(k) processing fee				$130	+0	139
24. If "assignment" box 6 is X'd, add recording fee.				$40	+40	581
25.				**TOTAL FEE ENCLOSED =**	**$440**	

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached.
This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed.

Pillsbury Madison & Sutro LLP
Intellectual Property Group
By: Atty: Paul N. Kokulis **Reg. No. 16773**

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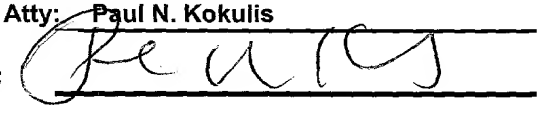
Sig: 

Fax: (202) 822-0944
Tel: (202) 861-3503

NOTE: File in duplicate with PTO receipt (PAT-103A) and attachments

08/913960

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

REQUEST FOR FILING NATIONAL PHASE OF PCT APPLICATION UNDER 35 U.S.C. 371 AND 37 CFR 1.494 OR 1.495

108 Rec'd PCT/PTO 25 SEP 1997

To: The Commissioner of Patents and Trademarks
Washington, D.C. 20231

(Our Deposit Account No. 03-3975)
(Our Order No. 41015/ 242267
C# / M#

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

Atty Dkt: 242267/ MBUS1126A
M#/Client Ref.

From: Cushman Darby & Cushman

Date: September 25, 1997

This is a **REQUEST** for **FILING** a PCT/USA National Phase Application based on:

1. International Application	2. International Filing Date	3. Earliest Priority Date Claimed
PCT/GB96/00575	19 MAR 1996	25 MAR 1995
⇧ country code	Day MONTH Year	Day MONTH Year (use item 2 if no earlier priority)

4. Measured from the earliest priority date in item 3, this PCT/USA National Phase Application Request is being filed within:

(a) ☐ 20 months from above item 3 date (b) ☒ 30 months from above item 3 date,

(c) Therefore, the due date (unextendable) is September 25, 1997

5. Title of Invention PHARMACEUTICAL COMPOSITION CONTAINING SELECTED LANTHANUM CARBONATE HYDRATES

6. Inventor(s) MURRER, Barry Anthony et al

Applicant herewith submits the following under 35 U.S.C. 371 to effect filing:

7. ☒ Please immediately start national examination procedures (35 U.S.C. 371 (f)).

8. ☐ **A copy of the International Application** as filed (35 U.S.C. 371(c)(2)) is transmitted herewith (file if in English but, if in foreign language, file only if not transmitted to PTO by the International Bureau) including:

a. ☐ Request;
b. ☐ Abstract;
c. _____ pgs. Spec. and Claims;
d. _____ sheet(s) Drawing which are ☐ informal ☐ formal of size ☐ A4 ☐ 13" ☐ 14"

9. ☒ **A copy of the International Application has been transmitted by the International Bureau.**

10. **A translation of the International Application** into English (35 U.S.C. 371(c)(2))
a. ☐ is transmitted herewith including: (1) ☐ Request; (2) ☐ Abstract;
(3) _____ pgs. Spec. and Claims;
(4) _____ sheet(s) Drawing which are:
☐ informal ☐ formal of size ☐ A4 ☐ 13" ☐ 14"
b. ☐ is not required, as the application was filed in English.
c. ☐ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.
d. ☐ Translation verification attached (not required now).

11 ☒ PLEASE AMEND the specification before its first line by inserting as a separate paragraph:
--This application is the national phase of international application PCT/GB96/00575, filed March 19, 1996 which designated the U.S.--

12. ☐ Amendments to the claims of the International Application **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., before 18th month from first priority date above in item 3, are transmitted herewith (file if in English but, if in foreign language, file only if not transmitted by the International Bureau) including:**

13. ☒ PCT Article 19 claim amendments (if any) have been transmitted by the International Bureau

14. ☐ Translation of the amendments to the claims **under PCT Article 19 (35 U.S.C. 371(c)(3)), i.e., of claim amendments** made before 18th month, **is attached (required by 20th month from the date in item 3 if box 4(a) above is X'd, or 30th month if box 4(b) is X'd, or else amendments will be considered canceled).**

15. **A declaration of the inventor** (35 U.S.C. 371(c)(4))
a. ☐ is submitted herewith ☐ Original ☐ Facsimile/Copy
b. ☐ is not herewith, but will be filed when required by the forthcoming PTO Missing Requirements Notice per Rule 494(c) if box 4(a) is X'd or Rule 495(c) if box 4(b) is X'd.

16. **An International Search Report (ISR):**
a. Was prepared by ☐ European Patent Office ☐ Japanese Patent Office ☐ Other
b. ☒ has been transmitted by the international Bureau to PTO.
c. ☐ copy herewith (___ pg(s).) ☐ plus Annex of family members (___ pg(s).).

17. **International Preliminary Examination Report** (IPER):
a. ☒ has been transmitted (if this letter is filed after 28 months from date in item 3) in English by the International Bureau with Annexes (if any) in original language.
b. ☐ copy herewith in English.
c.1 ☐ IPER Annex(es) in original language ("Annexes" are amendments made to claims/spec/drawings during Examination) including attached amended:
c.2 ☐ Specification/claim pages #_____ claims #
Dwg Sheets #
d. ☐ Translation of Annex(es) to IPER **(required by 30th month due date, or else annexed amendments will be considered canceled).**

18. **Information Disclosure Statement** including:
a. ☐ Attached Form PTO-1449 listing documents
b. ☐ Attached copies of documents listed on Form PTO-1449
c. ☒ A concise explanation of relevance of ISR references is given in the ISR.

19. ☐ **Assignment** document and Cover Sheet for recording are attached. Please mail the recorded assignment document back to the person whose signature, name and address appear at the end of this letter.

20. ☐ Copy of Power to IA agent.

21. ☐ **Drawings:** ___ sheet(s) per set: ☐ 1 set informal; ☐ Formal of size ☐ A4 ☐ 11"

22. ☐ _____ (No.) **Verified Statement(s)** establishing "small entity" status under Rules 9 & 27

23. **Priority** is hereby claimed under 35 U.S.C. 119/365 based on the priority claim and the certified copy, both filed in the International Application during the international stage based on the filing in (country) Great Britain of:

	Application No.	Filing Date		Application No.	Filing Date
(1)	9506126.3	25 MAR 1995	(2)		
(3)			(4)		
(5)			(6)		

a. ☒ See Form PCT/IB/304 sent to US/DO with copy of priority documents. If copy has not been received, please proceed promptly to obtain same from the IB.
b. ☐ Copy of Form PCT/IB/304 attached.

24. Attached:

25. **Preliminary Amendment:**

25.5 Per Item 17.c3, **cancel original** pages #_____, claims #_____, Drawing Sheets #

26. **Calculation of the U.S. National Fee (35 U.S.C. 371 (c)(1)) and other fees is as follows:**
based on amended claim(s) per above item(s) ☐ 12, ☐ 14, ☐ 17, ☐ 25, ☐ 25.5 (hilite)

Total Effective Claims	minus 20 =	x $22/$11	=	$	966/967
Independent Claims	minus 3 =	x $80/$40	=	$	964/965
If any proper (ignore improper) Multiple Dependent claim is present,		add$260/$130		+	968/969

BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(4)): →→**BASIC FEE REQUIRED NOW**→→

A. If country code letters in item 1 are not "US","BR","BB","TT","MX","IL" or "NZ"

See item 16a re:

1.	Search Report was not prepared by EPO or JPO - - - - - - - - -	add$1040/$520		960/961
2.	Search Report was prepared by EPO or JPO - - - - - - - - - - - -	add$910/$455	+910	970/971

SKIP B, C, D AND E UNLESS country code letters in item 1 are "US","BR","BB","TT","MX","IL" or "NZ"

(X) →	☐	B.	If neither international search fee nor international preliminary examination fee was paid to USPTO, - - - - -	add$1040/$520	+0	960/961
(Only) (one) → (Of)	☐	C.	If international search fee was paid to USPTO but not international preliminary examination fee, - - - - - - - - - - -	add$770/$385	+0	958/959
(these) (4) → (boxes)	☐	D.	If international preliminary examination fee was paid to USPTO -	add$700/$350	+0	956/957
→	☐	E.	If international preliminary examination fee was paid to USPTO and Rules 492(a)(4) and 496(b) satisfied,- - - - -	add $96/$48	+0	962/963

27.		**SUBTOTAL =**	$910
28.	If Assignment box 19 above is X'd, add Assignment Recording fee of $40	+0	(581)
29.	Attached is a check to cover the -	**TOTAL FEES**	$910

CHARGE STATEMENT: The Commissioner is hereby authorized to charge any fee specifically authorized hereafter, or any missing or insufficient fee(s) filed, or asserted to be filed, or which should have been filed herewith or concerning any paper filed hereafter, and which may be required under Rules 16-18 and 492 (missing or insufficient fee only) now or hereafter relative to this application and the resulting Official document under Rule 20, or credit any overpayment, to our Account/Order Nos. shown in the heading hereof for which purpose a duplicate copy of this sheet is attached.
This CHARGE STATEMENT does not authorize charge of the issue fee until/unless an issue fee transmittal form is filed

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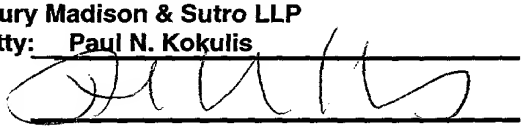
Sig: 
Fax: (202) 822-0944
Tel: (202) 861-3503

NOTE: File in duplicate with 2 postcard receipts (CDC-103) & attachments.

PHARMACEUTICAL COMPOSITION CONTAINING SELECTED LANTHANUM CARBONATE HYDRATES

This invention concerns a novel and inventive pharmaceutical composition and method, more particularly it concerns a composition for the treatment of hyperphosphataemia.

Hyperphosphataemia is a particular problem of patients with renal failure, using dialysis equipment. Conventional dialysis fails to reduce levels of phosphate in the blood, so that the levels rise in time. It is known to control phosphate levels by the oral administration of aluminium salts, or calcium salts. With the known toxic effects of aluminium, aluminium-based therapy tends to be avoided. In the case

of calcium salts, calcium is absorbed rather readily from the gut, and in turn causes hypercalcaemia.

It has been suggested (Nakagawa *et al*, Trans Am Soc Intern Organs, 31, (1985) 155-9) that hydrous cerium oxide could be used as a bead in an ion-exchange column, to bind phosphate during dialysis. Japanese published patent application 61 004 529 appears to cover the same idea, suggesting that the hydrous oxides of La, Ce and Y may be used in the column. However, although the rare earths are generally considered of low toxicity according to the Hodge-Sterner classification system (Am Ind Hyg Assoc Quart, 10, (1943), 93), their toxicity when given *iv*, which corresponds to use in a blood dialysis system, is significant and we are not aware that the suggested ion exchange system or any development thereof has met with widespread acceptance or has been tested clinically for hyperphosphataemia.

It appears that cerium oxide or oxalate was administered many years ago for different medical indications, but that this has fallen into complete disuse.

Japanese published patent application number 62-145024 (Asahi Chemical Ind KK) discloses that rare earth carbonates, bicarbonates or organic acid compounds may be used as phosphate binding agents. One example of said published application relates to the use of lanthanum carbonate, although in the tests described, cerium organic acid salts and carbonate gave better phosphate ion extraction than lanthanum carbonate. Example 11 of said published application prepares

$La_2(CO_3)_3.H_2O$, *ie* the monohydrate; all the other Examples are directed to rare earth carbonates other than lanthanum carbonate.

We have now discovered that certain forms of lanthanum carbonate exhibit improved performance in a variety of tests, over standard commercial lanthanum carbonate, which is believed to be the octahydrate form, and over $La_2(CO_3)_3.H_2O$ or similar compounds.

According to one aspect therefore, the present invention is the use of lanthanum carbonate of formula $La_2(CO_3)_3.xH_2O$ where x has a value from 3 to 6, preferably from 3.5 to 5, more especially from 3.8 to 4.5, for the preparation of a medicament for the treatment of hyperphosphataemia by administration into the gastrointestinal tract.

The invention further provides a pharmaceutical composition comprising said lanthanum carbonate, in admixture or association with a pharmaceutically acceptable diluent or carrier, in a form for administration into the gastrointestinal tract for the treatment of hyperphosphataemia.

The invention may also be expressed as a method of treatment of hyperphosphataemia in a patient with renal failure, comprising the administration of an effective dose of said lanthanum carbonate into the gastrointestinal tract.

According to another aspect, the present invention is a process for the preparation of lanthanum carbonate which comprises the steps of:

(i) reacting lanthanum oxide with an acid which gives a soluble salt of lanthanum;

(ii) reacting a solution of the thus obtained lanthanum salt with an alkali metal carbonate to produce a wet cake of lanthanum carbonate octahydrate; and

(iii) controlled drying of the wet cake of lanthanum carbonate octahydrate so as to obtain a lanthanum carbonate with 3 to 6 molecules of water of crystallisation.

According to yet another aspect, the present invention is lanthanum carbonate when obtained by the above-mentioned process.

According to a further aspect, the present invention is lanthanum carbonate of the formula $La_2(CO_3)_3.xH_2O$ where x has a value from 3 to 6.

Embodiments of the present invention are described below, by way of example only, with reference to the accompanying drawings in which:

Figure 1 illustrates the phosphate-binding capability of lanthanum carbonates having different degrees of water of crystallisation;

Figure 2 illustrates the drying curves for five batches of lanthanum carbonate prepared by the method indicated in Example 1;

Figure 3 illustrates the XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method indicated in Example 2; and

Figure 4 illustrates the XRD analysis of lanthanum carbonate $8.8H_2O$ of Sample 1 above.

For the tests described hereinafter, samples of lanthanum carbonate were obtained as follows:

Sample 1. Commercial lanthanum carbonate obtained from a chemical company. This was characterised by elemental analysis (La, C, H), TGA, X-ray powder diffraction and ir spectroscopy, to have the formula $La_2(CO_3)_3.8.8H_2O$.

Samples 2 - 4 were prepared by heating portions of Sample 1 at varying temperatures for varying lengths of time, either under vacuum or at atmospheric pressure to obtain materials of formula $La_2(CO_3)_3.xH_2O$ where $0 < x < 8$.

Sample	Initial wt (g)	Temp (°C)	Time (min)	Vacuum (Y/N)	Wt loss (g)	x
2	5.00	175	240	Y	1.09	1.3
3	20.0	80	180	N	2.6	4.4
4	5.01	100	720*	N	0.96	2.2

* Dried to constant weight.

Sample 5 is a sample of lanthanum carbonate which when analysed indicated a formula of $La_2(CO_3)_3.4H_2O$.

Sample 6 is a sample of lanthanum carbonate prepared according to Example 1 below and having the formula $La_2(CO_3)_3.3.8H_2O$.

In order to show that certain lanthanum carbonate hydrates are significantly different in phosphate binding activity from both lanthanum carbonate octahydrate and from $La_2(CO_3)_3.H_2O$, samples were tested as follows:

i) a stock solution was prepared by dissolving 13.75g of anhydrous Na_2HPO_4, 8.5g of NaCl in 1 litre deionised water.

ii) 100ml of the stock solution was adjusted to pH3 by the addition of concentrated HCl.

iii) A 5ml sample was taken and filtered through a 0.02μm filter to give a Time 0 sample. This was analysed for phosphate using a Sigma Diagnostics Colorimetric Phosphorus test kit.

iv) 5ml fresh stock solution was added to re-establish 100ml, and the pH was re-adjusted to approximately 3.

v) $La_2(CO_3)_3.xH_2O$ as a dry powder was added in an amount according to the molecular weight of the particular hydrate, to give a two-fold molar excess of lanthanum over phosphate and stirred at room temperature.

vi) Sampling was carried out at time intervals from 0.5 to 10 minutes, and the percentage of phosphate was determined as in iii) above. The results are shown in the Table 1 below.

TABLE 1

TIME (Minutes)	% PHOSPHATE REMOVED					
	Sample					
	1	2	3	4	5	6
0						
0.5		13.4	18.8	15.1	22.9	31.4
1	29	18.4	31.5	26.8	40.4	55.5
1.5		25.4	43.1	36	55.2	74.8
2		28.1	50.6	45.3	69.5	88.1
2.5		30.8	60.5	51.8	79.9	95.3
3		34.4	69	57.6	90.3	99.6
4						100
5	70.5	39.9	96.5	76.3	100	100
10	100	ND	99.1	ND	100	100

It can readily be seen from Table 1 that Sample 3 ($La_2(CO_3)_3.4.4H_2O$); Sample 5 ($La_2(CO_3)_3.4H_2O$) and Sample 6 ($La_2(CO_3)_3.3.8H_2O$) bind phosphate appreciably quicker than the $8.8H_2O$, $.1.3H_2O$ or $2.2H_2O$ forms. We believe that the results for $La_2(CO_3)_3.1.3H_2O$ are in agreement with the results shown in the above mentioned Japanese published patent application number 62-145024 where for $La_2(CO_3)_3.H_2O$, only 90% removal is shown after 120 minutes.

It can also be readily seen from Figure 1 of the accompanying drawings that the highest phosphate removal is obtained with lanthanum carbonates having 3 to 6 molecules of water.

The present invention offers the possibility of binding phosphate without any incursion of lanthanum into the blood stream, where toxic effects can cause problems. The specified lanthanum carbonate has negligible absorption from the gut, as shown by the *in vivo* tests described below.

Throughout this document, the term "treatment" is intended to include preventative treatment.

Processes for preparing lanthanum carbonates according to the present invention are described by way of illustration in the following Examples 1 and 2.

EXAMPLE 1

Lanthanum oxide (1.5kg, 4.58mol) was suspended in water (5.5 litres) in a 20 litre flask. Nitric acid (Analar grade, 69%, SG 1.42, 1.88 litres, 29.23mol) was added to the stirred solution over 1.5 hours at such a rate as to keep the temperature between 60-80°C. The resulting lanthanum nitrate solution was left to cool to room temperature and filtered. A solution of sodium carbonate (1.65kg, 15.57mol) in water (7.75 litres) was added to the stirred lanthanum nitrate solution over 45 minutes. At the end of the addition the pH of the suspension was 9.74. The suspension was left

overnight, filtered (Buchner funnel, 540 paper) and dried on the filter in a current of air for 30 minutes. The solid was then re-suspended in water, stirred for 40 minutes and filtered. This procedure was repeated to give a total of six washes, when the nitrate concentration in the filtrate was <500ppm. The final material (4.604kg) was divided between three Pyrex dishes and a sample from each analysed for water content. (By decomposition of weighed sample of $(La_2(CO_3)_3.xH_2O$ at 1050°C, 2 hours to La_2O_3). The dishes were then placed in a fan oven at 80°C and the weight loss of each dish monitored until the material of the required degree hydration was obtained. The progress of the drying is shown below

Time (hours)	mol H_2O/La		
	Dish 1	Dish 2	Dish 3
3.50	10.9	13.5	12.6
12	5.7	6.0	5.2
14	5.3	5.4	4.6
16	4.9	5.1	4.3
17	4.4	4.6	3.8
19.5	3.8	4.0	3.2

Drying curves for five batches produced by this route are shown in Figure 2.

$La_2(CO_3)_3.3.8H_2O$ from dish 1 was selected as Sample 6 for the phosphate binding tests set forth in Table 1.

EXAMPLE 2

The process of Example 1 was repeated but using hydrochloric acid (12.28M, 2.48 litres) in place of nitric acid to dissolve lanthanum oxide (1.5kg). The yield of crude product after six washes was 4.378kg. The product was divided in three approximately equal portions in Pyrex dishes and dried in a fan oven at 80°C. After 2 hours a sample was taken from each tray and water analysed by decomposition to lanthanum oxide as described above. These figures were used to calculate the weight loss needed to give material of the required composition. The time course of the drying process is shown below.

Time (hours)	mol H_2O/La		
	Dish 1	Dish 2	Dish 3
2	21.3	22.1	20.4
5.5	12.3	13.2	12.2
9	7.9	8.0	7.6
11.5	6.9	7.0	6.6
17	4.9	5.1	4.6
18.5	4.6	4.8	4.2
19.5	4.4	4.6	4.1
20	4.3	4.6	4.0

Samples were taken from each dish, combined and analysed. The following results were obtained:

	Found	Calculation for $La_2(CO_3)_3.4H_2O$
% La (gravimetric)	52.38%	52.4%
carbonate (titration)	5.76mol/g	5.66mol/g
H_2O (NMR)	13.06%	13.59%

The XRD analysis for lanthanum carbonate $4H_2O$ prepared by the method of Example 2 is illustrated in Figure 3.

Figure 4 illustrates the XRD of lanthanum carbonate $8.8H_2O$ and it is evident that it has a different crystalline structure from lanthanum carbonate $4H_2O$ prepared by the method of Example 2. The XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method of Example 1 was similar to the XRD analysis of lanthanum carbonate $4H_2O$ prepared by the method of Example 2.

Pharmaceutical compositions for oral administration according to the invention may be formulated and manufactured using methods well known in the art. Suitable diluents or carriers are also well known. The compositions may desirably be in a dosage form, to provide a single daily dose, or a number of sub-daily dosages. Conventional pharmacological methods may be used to ascertain suitable dose levels. The level of phosphate in the food that an individual ingests is important. Daily dosages are indicated to be in the range 0.1 to 50g, preferably about 0.5 to 15g. Suitable forms for oral administration include solid forms such as tablets, capsules and dragees and liquid forms such as suspensions or syrups. In addition to diluents and carriers, it is conventional in the formulation of oral preparations to include non-active

ingredients such as thickeners, taste-improving components and colouring agents. The said carbonate may also be coated or treated to provide delayed-release forms. Preferably, the required daily dosage is given in tablet form, *eg* chewable tablet form, to be taken with meals. A suitable daily dosage of about 2g for 70kg man, should be compared with a daily dosage of 20g for a commercial calcium-based phosphate binding composition.

To demonstrate that the lanthanum carbonate of the invention (or lanthanum phosphate formed after binding to phosphate in the gut) is fully excreted and does not pass out of the gut into the circulation system when given orally, three rats were dosed with 20mg/kg of $La_2(CO_3)_3.4H_2O$ (Sample 5) and kept in metabolic cages where faeces and urine could be collected. The results are shown in Table 2 below.

Animal No.	Time (hours)	% La Recovered
1	24	103.2
1	48	0.1
1	72	<0.2
1	Total	103.3
2	24	75.3
2	48	23
2	72	1.2
2	Total	99.5

Animal No	Time (hours)	%La Recovered
3	24	93.8
3	48	10
3	72	0.1
3	Total	103.8

It can be seen that after 72 hours, all of the lanthanum has been excreted. In the urine samples, the amount of lanthanum was below detection limits. After the test, the rats were sacrificed, and kidney, liver and femur were analysed for lanthanum. In all cases, the amount of lanthanum was below 0.1ppm.

CLAIMS

1. A pharmaceutical composition for the treatment of hyperphosphataemia, comprising lanthanum carbonate of formula

$$La_2(CO_3)_3.xH_2O$$

where x has a value from 3 to 6, in admixture or association with a pharmaceutically acceptable diluent or carrier.

2. A composition according to claim 1, wherein in the lanthanum carbonate, x has a value from 3.5 to 5.

3. A composition according to claim 2, wherein in the lanthanum carbonate, x has a value from 3.8 to 4.5.

4. A composition according to any one of claims 1 to 3, in a form suitable for oral administration.

5. A composition according to any one of claims 1 to 4 in unit dosage form to provide from 0.1 to 20g/day.

6. The use of lanthanum carbonate as defined in any one of claims 1 to 3, for the preparation of a medicament for the treatment of hyperphosphataemia by administration into the gastrointestinal tract.

Art. 34 Amendment

7. A process for the preparation of lanthanum carbonate as defined in any one of claims 1 to 3 which comprises the steps of:

(i) reacting lanthanum oxide with hydrochloric acid to obtain lanthanum chloride;

(ii) reacting a solution of the thus obtained lanthanum chloride with an alkali metal carbonate to produce a wet cake of lanthanum carbonate octahydrate; and

(iii) controlled drying of the wet cake of lanthanum carbonate octahydrate so as to obtain a lanthanum carbonate with 3 to 6 molecules of water of crystallisation.

8. A process as claimed in claim 7 wherein the alkali metal carbonate is sodium carbonate.

9. Lanthanum carbonate prepared according to the process of claim 7 or 8.

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Fig. 1

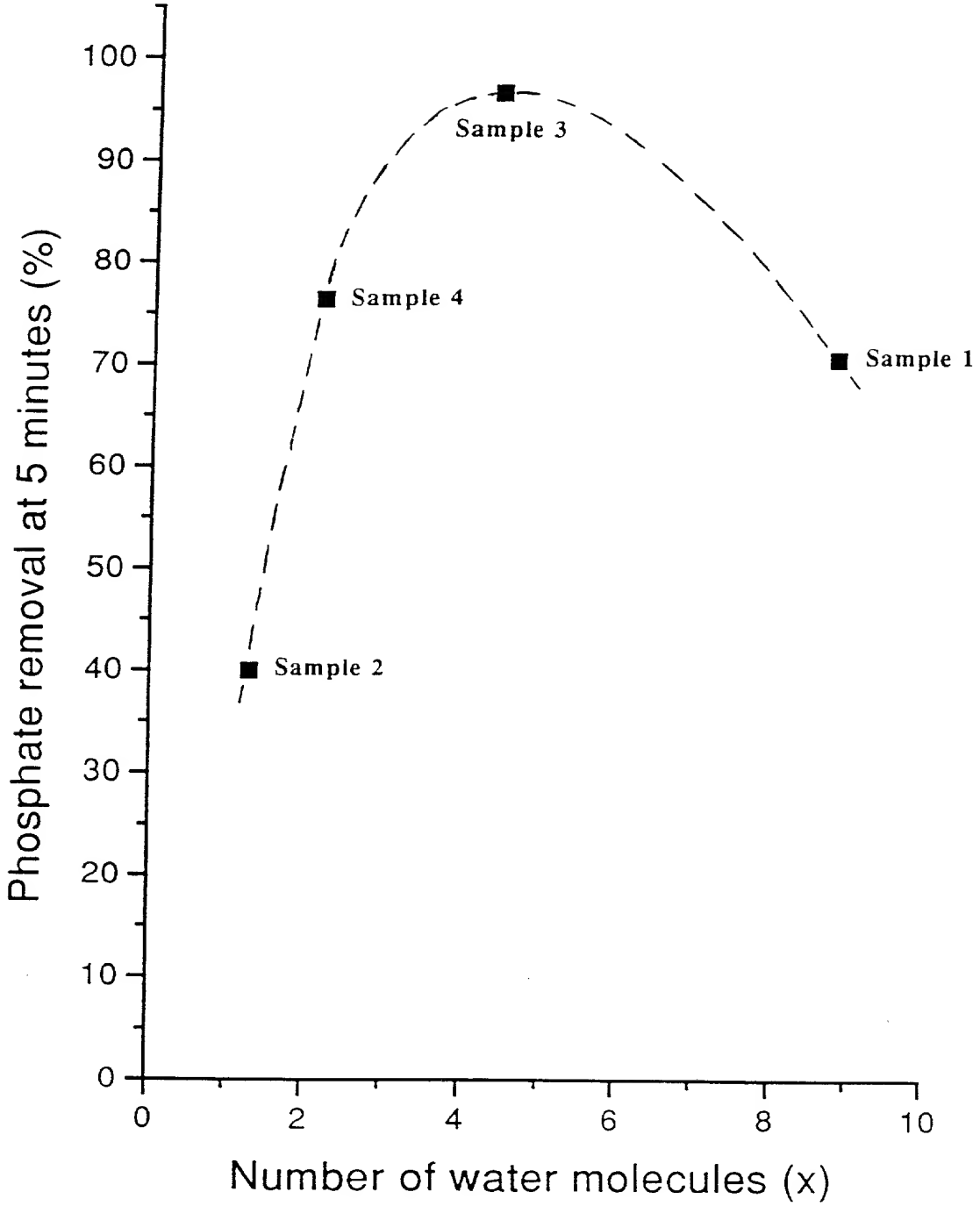


Fig. 2

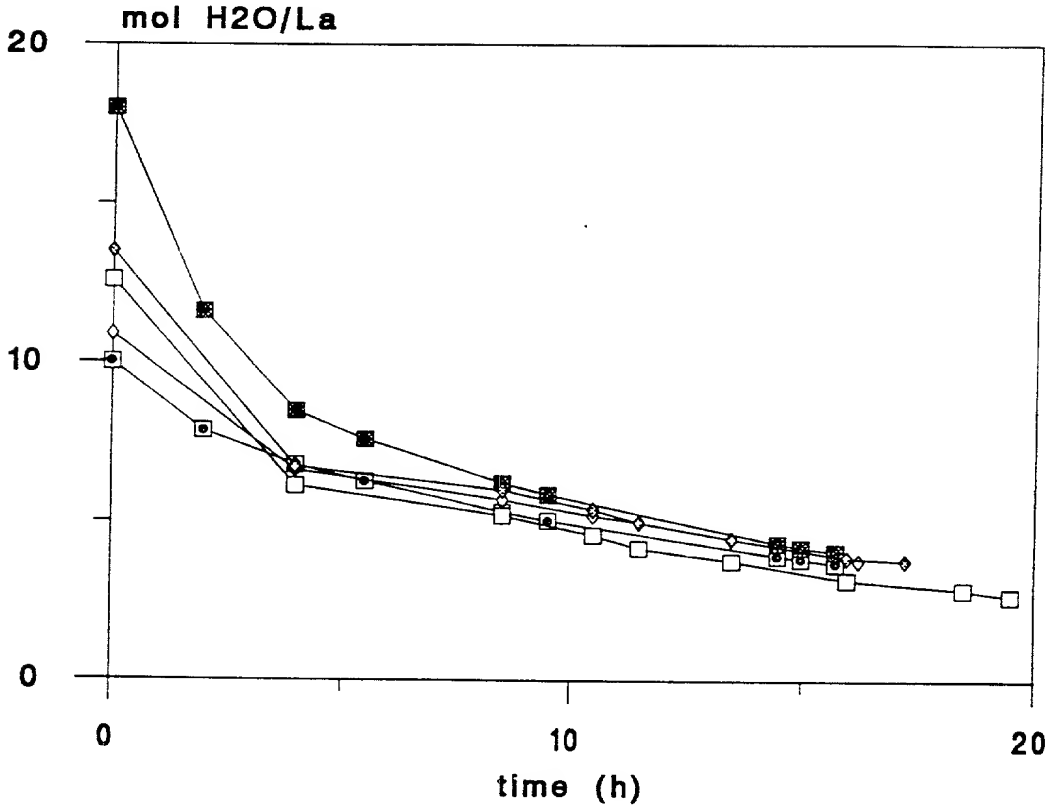


Fig. 3

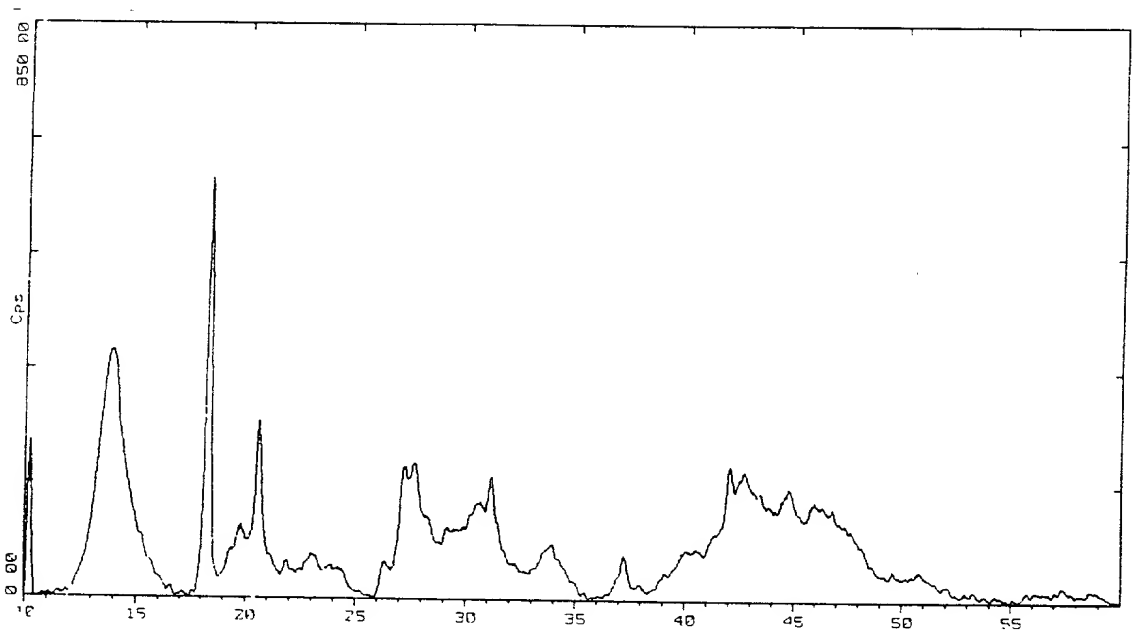
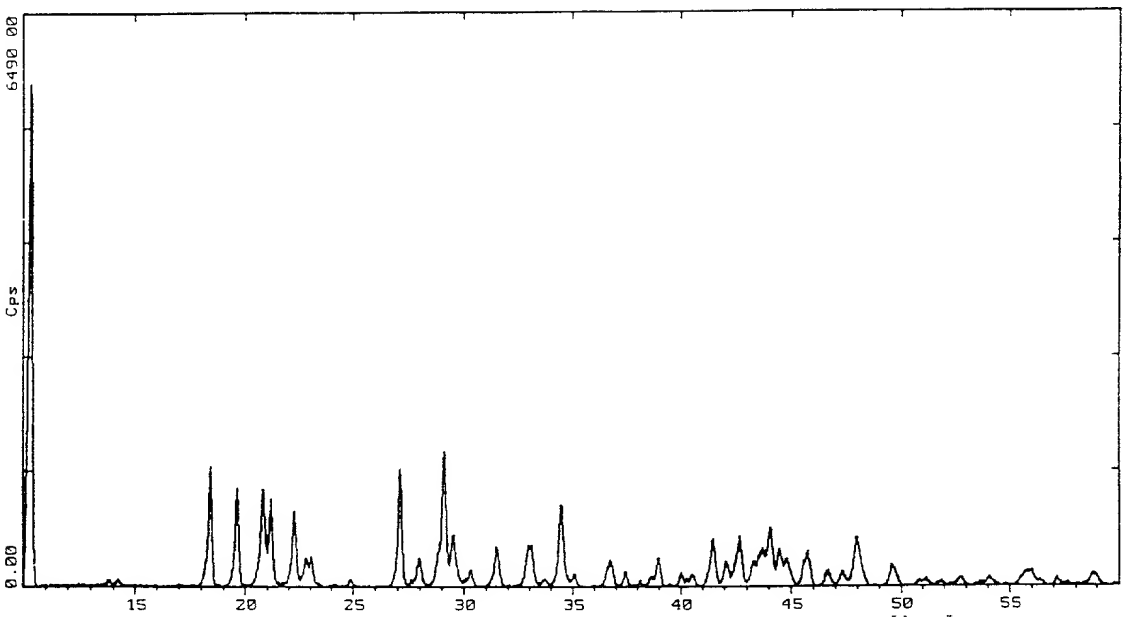


Fig.4



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FOR UTILITY/DESIGN
CIP/PCT NATIONAL/PLANT
ORIGINAL/SUBSTITUTE/SUPPLEMENTAL
DECLARATIONS

RULE 63 (37 C.F.R. 1.63) DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CUSHMAN FORM

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the **INVENTION ENTITLED** PHARMACEUTICAL COMPOSITION CONTAINING SELECTED LANTHANUM CARBONATE HYDRATES

the specification of which (CHECK applicable BOX(ES))

-> [X] is attached hereto.

X -> [ ] was filed on _____ as U.S. Application No. 0_/_____

BOX(ES) -> [X] was filed as PCT International Application No. PCT/ GB96 / 00575 on 19 March 1996

-> -> and (if applicable to U.S. or PCT application) was amended on 12 February 1997

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C.119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing date of this application:

PRIOR FOREIGN APPLICATION(S) Number	Country	Day/MONTH/Year Filed	Date first Laid-open or Published	Date Patented or Granted	Priority Claimed Yes	No
9506126.3	GB	25 March 1995			Yes	

I hereby claim domestic priority benefit under 35 U.S.C.120/365 of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

PRIOR U.S. PROVISIONAL, NONPROVISIONAL AND/OR PCT APPLICATION(S) Application No. (series code/serial no.)	Day/MONTH/Year Filed	Status pending, abandoned, patented	Priority Claimed Yes	No

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

And I hereby appoint Cushman Darby & Cushman, L.L.P., 1100 New York Avenue, N.W., Ninth Floor, East Tower, Washington, D.C. 20005-3918, telephone number (202) 861-3000 (to whom all communications are to be directed), and the below-named persons (of the same address) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete names/numbers below of persons no longer with their firm and to act and rely on instructions from and communicate directly with the person/ assignee/ attorney/ firm/ organization who/ which first sends/ sent this case to them and by whom/ which I hereby declare that I have consented after full disclosure to be represented unless/ until I instruct Cushman Darby & Cushman in writing to the contrary.

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1. INVENTOR'S SIGNATURE: _____ Date 23/9/97

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3. INVENTOR'S SIGNATURE: _____ Date _____

Inventor's Name (typed) _____ (First) (Middle Initial) (Family Name) (Country of Citizenship)

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(FOR ADDITIONAL INVENTORS, check box [ ] and attach sheet (CDC-116.2) for same information for each re signature, name, date, citizenship, residence and address.)